REMARKS

Upon entry of these amendments, claims 1, 4-5, 9-17, 35, 38-39, 43-51, 53, and 73-76 are pending in the instant application. Claims 1, 35 and 53 are amended. Support for these amendments can be found throughout the specification, for example, at page 6, lines 3-11; page 7, lines 10-13; page 11, lines 24-32 and page 13, lines 21-29. No new matter is added.

Claim Listing

Applicants note, with appreciation, the Examiner's comments at pages 2-3 regarding the error in the claim listing of January 3, 2008. Applicants apologize for this oversight and will be sure to comply with the guidelines of 37 C.F.R. §1.121(c) in future communications with the office.

Rejections Under 35 U.S.C. §112, First Paragraph

Written Description

Claims 1, 4-5, 9-17, 35, 38-39, 43-51 and 73-76 are rejected under 35 USC §112, first paragraph, as failing to comply with the written description requirement. The Examiner asserts that the concept of elevation of the specific E2F factors E2F-1, E2F-2 and E2F-3 with any G1 or S phase checkpoint activator compound is not supported by the instant specification. *See*, Office Action at pages 4-5. Applicants respectfully disagree.

The specification describes at page 6, line 8 - page 7, line 9 that any cell cycle checkpoint activation modulator can be administered to elevate the level of a member of the E2F family of transcription factors (including but not limited to E2F-1, E2F-2 or E2F-3). The specification further describes that a cell cycle checkpoint activation modulator can be a G1 or S phase checkpoint activation modulator and that preferred checkpoint activation modulators are 3,4-dihydro-2,2-dimethyl-3-(3-methyl-2-butenyl)-2H-naphtho[1,2-b]pyran-5,6-dione, 3,4-dihydro-2,2-dimethyl-2H-naphtho[1,2-b]thiopyran-5,6-dione and 3,4-dihydro-4,4-dimethyl-2H-naphtho[1,2-b]thiopyran-5,6-dione.

As such, Applicants submit that the instant specification readily conveys to one of ordinary skill in the art that applicants were in possession of the currently claimed invention at the time of filing. Reconsideration and withdrawal are requested.

Enablement

Claims 1, 4-5, 9-17, 35, 38-39, 43-51, 53 and 73-76 are rejected under 35 USC §112, first paragraph, for scope of enablement. The Examiner asserts that the instant specification does not provide enablement for the administration of a G1 or S phase checkpoint activator to elevate the expression of an E2F transcription factor (selected from E2F-1, E2F-2 or E2F-3) in cancerous cells but not affecting the viability of non-cancerous cells. More specifically, the Examiner asserts that more guidance is required to describe to the skilled artisan how to elevate E2F transcription factors in cancerous cells without causing toxicity in non-cancer cells in view of the state of the art at the time of filing. *See*, Office Action at pages 5-7.

The Examiner further states that while the specification demonstrates a clear elevation of E2F transcription factor expression in cancerous cells versus non-cancerous cells, the instant specification fails to provide any specific direction or guidance as to how one would effectively administer the claimed G1 or S phase checkpoint activator to achieve elevation of E2F expression and selectively induce toxicity in cancer cells only. Specifically, the Examiner states that the instant disclosure lacks clear direction how the skilled artisan would execute the methods of the instant claims *without* causing toxicity in, or affecting the viability of, any non-cancerous cell(s) in the subject to be treated (*emphasis in original*). *See*, Office Action at page 8. More specifically, the Examiner asserts that Applicants have failed to rebut the presumption of unpredictability and complexity in the art. *See*, Office Action at page 9. Applicants disagree.

The present invention readily describes that the G1 or S phase checkpoint activator of the present invention are capable of selectively elevating an E2F transcription factor (selected from E2F-1, E2F-2 or E2F-3), selectively activating a G1 or S phase checkpoint to selectively induce apoptosis in a cancer cell, without elevation of E2F, activation of a G1 or S phase checkpoint and induction of apoptosis in non-cancerous cells. *See*, instant specification, *inter alia*, at Example 2 beginning at page 34, line 9 - page 36, line 6, as well as Figures 7-11 and Table 1. Moreover, as

described previously, the application provides therapeutically effective dosage ranges for use in the instant invention at page 29, line 26, to page 30, line 6. Applicants submit that determining the specific amount necessary to administer for a specific subject is well within the art of the appropriate clinician or practitioner in view of the instant application. Reconsideration and withdrawal are requested.

Claim Rejections Under 35 USC §102

Claims 1, 4-5, 9-17, 35, 38-39, 43-51, 53 and 73-76 are rejected under 35 USC §102(a) as being anticipated by Jiang et al. (WO 03/011224), herein referred to as "Jiang," in light of Jacob ("Paclitaxel," Pharmacology, 4th Ed., 1996; p. 268), herein referred to as "Jacob." Applicants traverse the rejection with respect to the claims as amended herein.

Claims 1, 35 and 53 (from which the remaining claims subject to the rejection depend) are amended to recite that the G1 or S phase checkpoint activator is administered to:

- elevate the expression of a member of the E2F family of transcription factors (*e.g.*, E2F-1, E2F-2 and E2F-3), in cancerous cells but not in non-cancerous cells;
- activate a G1 or S phase checkpoint in cancerous cells but not in non-cancerous cells; and
- induces apoptosis in cancerous cells but not in non-cancerous cells.

Jiang (in light of Jacob) does not teach or suggest, explicitly or inherently, the administration of a G1 or S phase checkpoint activator which will selectively elevate an E2F transcription factor (selected from E2F-1, E2F-2 or E2F-3), selectively activate a G1 or S phase checkpoint and selectively induce apoptosis in cancerous cells, without elevating of E2F, activating a G1 or S phase checkpoint or inducing apoptosis in non-cancerous cells, wherein the G1 or S phase checkpoint activator is not β-lapachone, as required by the instant claims. Reconsideration and withdrawal are requested.

Claim Rejections Under 35 USC §103

Claims 1, 15-17, 35, and 49-51 remain rejected under 35 USC §103(a) as being

unpatentable over Jiang in view of Pardee et al. (WO 00/61142), herein referred to as "Pardee." Applicants traverse the rejection with respect to the claims as amended herein.

As described *supra*, Jiang does not teach or suggest, explicitly or inherently, the administration of a G1 or S phase checkpoint activator which will selectively elevate an E2F transcription factor (selected from E2F-1, E2F-2 or E2F-3), selectively activate a G1 or S phase checkpoint and selectively induce apoptosis in cancerous cells, without elevating of E2F, activating a G1 or S phase checkpoint or inducing apoptosis in non-cancerous cells, wherein the G1 or S phase checkpoint activator is not β-lapachone, as required by the instant claims.

Pardee does not cure these deficiencies of Jiang. Pardee merely teaches the administration of G1 and/or S phase drugs in combination with a variety of G2/M phase drugs for the treatment of various cancers. Pardee does not teach or suggest the administration of a G1 or S phase checkpoint activator which will selectively elevate an E2F transcription factor (selected from E2F-1, E2F-2 or E2F-3), selectively activate a G1 or S phase checkpoint and selectively induce apoptosis in cancerous cells, without elevating of E2F, activating a G1 or S phase checkpoint or inducing apoptosis in non-cancerous cells, wherein the G1 or S phase checkpoint activator is not β-lapachone, as required by the instant claims. As such, the combination of Jiang and Pardee does not teach or suggest all the limitations of the pending claims and one of ordinary skill in the art would be unable to combine Jiang and Pardee to reach the claimed invention with predictable results. Reconsideration and withdrawal are requested.

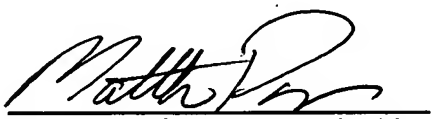
Double Patenting

Claims 1, 4-5, 9-17, 35, 38-39, 43-51, 53 and 73-74 remain provisionally rejected under the judiciously created doctrine of obviousness-type double patenting as being unpatentable over the method claims contained within U.S. Patent Application Nos. 10/887,009; 11/068,459; and 11/069,637. Applicants will address these rejections upon notice of allowable subject matter in the instant application.

CONCLUSION

On the basis of the foregoing amendment and remark, Applicants respectfully submit that the pending claims are in condition for allowance. Should any questions or issues arise concerning this application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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